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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,687	11/21/2001	Luisa Iruela-Arispe	1488.107000D/EKS/CML	9708

22195 7590 03/10/2006

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,687	IRUELA-ARISPE ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1-3,5-7 and 9-32 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-3,5-7 and 9-32 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 6, 2005 has been entered.

2. Claims 1, 2, 5 and 6 have been amended.. Claims 1-3, 5-7 and 9-32 are pending and under consideration.

3. Sections of Title 35, US Code not found in this action can be found in a prior action.

4. Claim 1 is objected to for the typographical error of "Syndrom" rather than "Syndrome".

5. Claims 1-3, 5-7 and 9-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claims 1, 2, 5 and 6 have been amended to incorporate the limitation "wherein said polypeptide is capable of inhibiting angiogenesis" in order to comply with the written description requirement. However, the added subject matter is not supported by the original disclosure. As stated in the previous rejection, amino acids 214-439 contain the metalloprotease domain of METH2; amino acids 440-529 contain the disintegrin domain of METH2; amino acids 530-583 contain a first TSP-like domain of METH2; and amino acids 837-890 contain the second TSP-like domain of METH2. The specification states on page 5, lines 3-4 that peptide and recombinant proteins derived from the TSP-like domain of METH1 and METH2 blocked VEGF-induce angiogenesis. This does not provide support for polypeptides which minimally comprise amino acid residues outside of the TSP-like domains having the characteristic of being capable of inhibiting angiogenesis, such as residues 214-239 and 440-529.

6. Claims 1-3, 5-7 and 9-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 1 , 3, 5, 7 and 9-20 are drawn to a method of treating an individual comprising administration of the various polypeptides comprising fragments of SEQ ID NO:2 and SEQ ID NO:4 recited in the claims, wherein the polypeptides are capable of inhibiting angiogenesis, and wherein said method is used to treat benign tumors, an ocular angiogenic disease, vasculogenesis, granulations, hypertrophic scars, nonunion fractures, scleroderma, trachoma, vascular adhesions, myocardial angiogenesis, coronary collaterals, cerebral collaterals, arteriovenous malformations, ischemic limb angiogenesis, Osler-Webber Syndrome, plaque neovascularization, hemophiliac joints, angiofibroma, fibromuscular dysplasia, wound granulation, or atherosclerosis. Claims 2, 6 and 21-32 are drawn to the treatment of an individual comprising administration of the various polypeptides comprising fragments of SEQ ID NO:2 and SEQ ID NO:4 recited in the claims, wherein the polypeptides are capable of inhibiting angiogenesis, and wherein said method is used as birth control. The specification

provides an experimental model system for the demonstration of anti-angiogenic activity. The specification does not provide objective evidence of the treatment of an individual suffering from any of the diseases or syndromes recited in claims 1 and 5 (description of Figures 6 and 7). The specification does not provide objective evidence that the administration of the claimed polypeptides could function as a birth control treatment. The instant claims encompass the treatment of an angiogenesis-mediated disease or tumor in a human patient in need thereof and the use of the claimed polypeptides as inhibiting angiogenesis effective as a birth control means. The demonstration that the instant peptides inhibits angiogenesis in the models used in the specification does not provide enablement for the treatment of any of all of the angiogenesis-mediated disease listed in claims 1, 2, 5 and 6, nor does it provide enablement for a method for inhibiting tumor metastasis or angiogenesis from a tumor arising in situ in an individual in need thereof because more teachings are required than the simple ability to inhibit angiogenesis when provided in a given concentration in an assay system because there is no teachings on the amounts of peptides required for the inhibition of the various diseases claimed, nor are there teachings regarding the duration of treatment necessary in order to produce an anti-angiogenic effect for all the diseases claimed nor are there teachings for the concentration of peptides necessary, and the length of exposure of the tissue or tumor necessary to inhibit solid tumors or tumor metastasis. Further, there are not teachings regarding the plasma concentration, tissue localization or the appropriate timing and duration of the treatment necessary to function in birth control. The art teaches general problems with the administration of peptide and protein drugs, namely short half-life in vivo, necessitating multiple administrations (Johnson and Tracey, 'Peptide and Protein Drug Delivery', In: Encyclopedia of Controlled Drug Delivery, Vol. 2, 1999, pages 816-833). The art teaches that major stability, release and manufacturing challenges" (page 816, second column, lines 1-5) must be met in order to overcome the technical difficulties associated with the delivery of peptides in vivo, because of the necessity of supplying repeated or sustained dosages over time necessary to overcome the short half-life in vivo. The art teaches that considerations in formulating the delivery of repeated or sustained dosages of peptides are stabilization of the peptides from degradation in vivo, and stabilization of peptides during the manufacturing process, and the subsequent controlled release of said stabilized peptides in vivo in the appropriate quantities. The specification does not teach a

means for the delivery of these small peptides to the all the disease sites encompassed by all the angiogenesis-mediated diseases claimed, such that the level of peptide is maintained for the time required to produce efficacy against said angiogenesis-mediated diseases, or to inhibition tumor-growth or tumor metastasis in a patient, in order to function as a birth control agent. Therefore it would be undue experimentation in order for one of skill in the art to determine a means for the delivery of the peptides to the tumor in a patient in such quantities which would be efficacious to said patient, wherein said delivery means would include how to stabilize the peptides from degradation in vivo, or during the manufacturing process, and how to release the stabilized peptides in vivo in the appropriate quantities. Given the lack of teachings on all of the above, one of skill in the art would be subject to undue experimentation in order to carry out the instant methods by administering the claimed polypeptides.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
3/6/2006

KAREN A. CANELLA PH.D
PRIMARY EXAMINER